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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,874	11/03/2003	Arthur Kunz	AM100788 P1	4900

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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,874	KUNZ ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-144* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-144* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Restriction Requirement mailed on 08/10/2005 has been withdrawn because claims 75-76 and 103-106 were not presented. The Restriction Requirement, including claims 75-76 and 103-106, is presented below.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-2, 11-27, 65-77, 78 and 79-90, as specifically drawn to a method of preparing monomeric cytotoxic drug/carrier conjugates with reduced low conjugated fraction (LCF) comprising a proteinaceous carrier, a linker and a cytotoxic drug, wherein the proteinaceous carrier is a hormone, classified in class 530, subclass 402.

II. Claims 1-2, 11-27, 65-77, 78 and 79-90, as specifically drawn to a method of preparing monomeric cytotoxic drug/carrier conjugates with reduced low conjugated fraction (LCF) comprising the a proteinaceous carrier, a linker and a cytotoxic drug, wherein the proteinaceous carrier is a growth factor, classified in class 530, subclass 402.

III. Claims 1-2, 3, 4, 5, 6, 11-27, 65-77, 78 and 79-90, as specifically drawn to a method of preparing monomeric cytotoxic drug/carrier conjugates with reduced low conjugated fraction (LCF) comprising the a proteinaceous carrier, a linker and a cytotoxic drug, wherein the proteinaceous carrier is an antibody comprising SEQ ID NO: 19 and 27, classified in class 530, subclass 402.

IV. Claims 1-2, 3, 4, 5, 7-9, 11-27, 65-77, 78 and 79-90, as specifically drawn to a method of preparing monomeric cytotoxic drug/carrier conjugates with reduced low conjugated fraction (LCF) comprising the a proteinaceous carrier, a linker and a cytotoxic drug, wherein the proteinaceous carrier is an antibody comprising SEQ ID NO: 28 and 30, classified in class 530, subclass 402.

V. Claims 1-2, 3, 4, 5, 10-27, 65-77, 78 and 79-90, as specifically drawn to a method of preparing monomeric cytotoxic drug/carrier conjugates with reduced low conjugated fraction (LCF) comprising the a proteinaceous carrier, a linker and a cytotoxic drug, wherein the proteinaceous carrier is a variant antibody obtained by an affinity maturation protocol and has increased specificity for human CD22, classified in class 530, subclass 402.

VI. Claims 28-32, 33, 37-42, 43-44, 48, 54, 61-64, 91-92, 93-98, 102 and 107-112, as specifically drawn to a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody comprising SEQ ID NO: 19 and 27, classified in class 530, subclass 391.7.

VII. Claims 28-32, 34-42, 43-44, 48, 55-57, 61-64, 91-92, 93-98, 103-105 and 107-112, as specifically drawn to a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody comprising SEQ ID NO: 28 and 30, classified in class 530, subclass 391.7.

VIII. Claims 43-44, 45, 46, 47, 61-64, 91-92, 93-98, 99-100, 101, 107-112, as specifically drawn to a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody, classified in class 530, subclass 391.7. (Upon the election of Group VII, Applicant must choose **ONE** amino acid SEQ ID NO from claims 45, 46 and 47, as each SEQ ID NO is a distinct invention, NOT a species.)

IX. Claims 43-44, 48, 49-51, 61-64, 91-92, 93-98, 99-100, 101, 107-112, as specifically drawn to a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody comprising a variable domain comprising a human acceptor framework regions and non-human donor residues at positions 1, 28, 48, 71 and 93, classified in class 530, subclass 391.7.

X. Claims 43-44, 48, 52-53, 61-64, 91-92, 93-98, 99-100, 101, 107-112, as specifically drawn to a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody comprising a variable domain comprising a human acceptor framework regions and non-human donor residues at positions 67 and 69, classified in class 530, subclass 391.7.

XI. Claims 43-44, 48, 58, 61-64, 91-92, 93-98, 99-100, 101, 106, 107-112, as specifically drawn to a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is a variant antibody obtained by an affinity maturation protocol and has increased specificity for human CD22, classified in class 530, subclass 391.7.

XII. Claims 43-44, 59, 61-64, 91-92, 93-98, 99-100, 101, 107-112, as specifically drawn to a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is a chimeric antibody comprising the amino acid sequence of SEQ ID NO: 7 and 8, classified in class 530, subclass 391.7.

XIII. Claims 43-44, 60-64, 91-92, 93-98, 99-100, 101, 107-112, as specifically drawn to a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody comprising a hybrid CDR comprising a truncated donor CDR sequence wherein the missing portion of the donor CDR is replaced by a different sequence and forms a functional CDR, classified in class 530, subclass 391.7.

XIV. Claims 113-127, 128, 129, 130, 131, 132, 133, 134, 135, 142, 143-144, as specifically drawn to a method of treating a subject with a proliferative disorder, comprising administering a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/carrier conjugate with one or more bioactive agents, wherein the bioactive agent is an antibody, classified in class 424, subclass 181.1.

XV. Claims 113-127, 128, 129, 130, 131, 136, 143-144, as specifically drawn to a method of treating a subject with a proliferative disorder, comprising administering a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/carrier conjugate with one or more bioactive agents, wherein the bioactive agent is a growth factor or cytokine, classified in class 424, subclass 181.1.

XVI. Claims 113-127, 128, 129, 130, 131, 137, 143-144, as specifically drawn to a method of treating a subject with a proliferative disorder, comprising administering a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/carrier conjugate with one or more bioactive agents, wherein the bioactive agent is a hormone, classified in class 424, subclass 181.1.

XVII. Claims 113-127, 128, 129, 130, 131, 143-144, as specifically drawn to a method of treating a subject with a proliferative disorder, comprising administering a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/carrier conjugate with one or more bioactive agents, wherein the bioactive agent is an anti-hormone, classified in class 424, subclass 181.1.

XVIII. Claims 113-127, 128, 129, 130, 131, 143-144, as specifically drawn to a method of treating a subject with a proliferative disorder, comprising administering a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/carrier conjugate with one or more bioactive agents, wherein the bioactive agent is a xanthine, classified in class 424, subclass 181.1.

XIX. Claims 113-127, 128, 129, 130, 131, 143-144, as specifically drawn to a method of treating a subject with a proliferative disorder, comprising administering a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/carrier conjugate with one or more bioactive agents, wherein the bioactive agent is an interleukin, classified in class 424, subclass 181.1.

XX. Claims 113-127, 128, 129, 130, 131, 143-144, as specifically drawn to a method of treating a subject with a proliferative disorder, comprising administering a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/carrier conjugate with one or more bioactive agents, wherein the bioactive agent is an interferon, classified in class 424, subclass 181.1.

XXI. Claims 113-127, 128, 129, 130, 131, 138, 139, 140, 141, 143-144, as specifically drawn to a method of treating a subject with a proliferative disorder, comprising administering a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/carrier conjugate with one or more bioactive agents, wherein the bioactive agent is a cytotoxic drug, classified in class 424, subclass 181.1.

The inventions are distinct, each from the other because of the following reasons:

The inventions of Groups VI-XIII represent separate and distinct products which are made by materially different methods, and are used in materially different methods which have different modes of operation, different functions and different effects. In the instant case, a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody comprising SEQ ID NO: 19 and 27 (Group VI), the monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody comprising SEQ ID NO: 28 and 30 (Group VII), a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody (Group VIII), a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody comprising a variable domain comprising a human acceptor framework regions and non-human donor residues at positions 1, 28, 48, 71 and 93 (Group IX), a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody comprising a variable domain comprising a human acceptor framework regions and non-human donor residues at positions 67 and 69 (Group X), a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is a variant antibody obtained by an affinity maturation protocol and has increased specificity for human CD22 (Group XI), a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is a chimeric antibody comprising the amino acid sequence of SEQ ID NO: 7 and 8 (Group XII) and a monomeric cytotoxic drug derivative/carrier conjugate, wherein the carrier is an antibody comprising a hybrid CDR comprising a truncated donor CDR sequence wherein the missing portion of the donor CDR is replaced by a different sequence and forms a functional CDR (Group XIII) are all structurally and/or chemically and/or functionally distinct compounds such that one invention could not be interchanged with the other. For these reasons the inventions of Groups VI-XIII are patentably distinct.

Furthermore, searching the inventions of Groups VI-XIII would impose a serious search burden. Currently, there are approximately eight different databases that accompany the results of a

search for one discrete amino acid sequence or nucleotide sequence and each result set from a particular database must be carefully considered. Hence, the search for every different amino acid sequence and every different amino acid segments in the databases, in addition to searching the organic molecule databases would require extensive searching and review.

The inventions of Groups I-V and XIV-XXI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the specification does not disclose that their methods would be used together. The methods of preparing a monomeric cytotoxic drug/carrier conjugate (Groups I-V) and the methods of treating a subject with a proliferative disorder (Groups XIV-XXI) are unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. Each invention performs this function using structurally and functionally divergent material. Moreover, the methodology and materials necessary for the preparation and treatment differ significantly for each of the materials. For preparing a monomeric cytotoxic drug/conjugate, a hormone, growth factor, antibody comprising SEQ ID NOs: 19 and 27 or an antibody comprising SEQ ID NOs: 28 and 30 may be used. For treating, a hormone, growth factor, antibody , anti-hormone, interleukin, interferon or a xanthine may be used. Therefore, each method is divergent in materials and steps. For these reasons the inventions of Groups I-V and XIV-XXI are patentably distinct.

Furthermore, the distinct steps and products require separate and distinct searches. The inventions of Groups IV and VI-X have a separate status in the art as shown by their different classifications. As such, it would be burdensome to search the inventions of Groups IV and VI-X.

The inventions of Groups VI-XIII and XIV-XXI are related as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the method of treating a proliferative disorder can be practiced with another materially different product such as a composition comprising a

monomeric cytotoxic drug derivative and a hormone or a anti-hormone or an antibody or a xanthine, or an interleukin, or an interferon or a cytotoxic agent.

The inventions of Groups III-V and VI-VII, XI are related as processes of making and products made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the process as claimed can be used to make other and materially different products such as a monomeric cytotoxic drug/carrier conjugate wherein the proteinaceous carrier is a hormone or a growth factor.

Because the inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the search required for each group is not required for other groups because each group requires a different non-patent literature search due to each group comprising different products and/or method steps, restriction for examination purposes as indicated is proper.

Species Election

This application contains claims directed to the following patentably distinct species of the claimed invention:

Claim 15, Groups I-V, is generic to a plurality of disclosed patentably distinct species comprising the following cytotoxic drugs: calicheamicins, thiotepa, taxanes, vincristine ... hemiasterlins and maytansinoids which differ at least in mechanism of action and chemical structure such that one species could not be interchanged with another.

Claim 77, Groups I-V, is generic to a plurality of disclosed patentably distinct species comprising the following cryoprotectant: alditol, mannitol, sorbitol ...glycerol, and pentaerythitol which differ at least in chemical properties and/or chemical structure such that one species could not be interchanged with another.

Claim 128, Groups XIV-XXI, is generic to a plurality of disclosed patentably distinct species comprising the following cytotoxic drugs: calicheamicins, thiotepa, taxanes, vincristine ... maytansinoids and esperamicins which differ at least in mechanism of action and chemical structure such that one species could not be interchanged with another.

Claim 138, Groups XIV-XXI, is generic to a plurality of disclosed patentably distinct species comprising the following cytotoxic drugs: doxorubicin, daunorubicin, idarubicin... taxol analogs and mitomycin which differ at least in mechanism of action and chemical structure such that one species could not be interchanged with another.

Claims 139, 140, 141, and 142, Groups XIV-XXI, are generic to a plurality of disclosed patentably distinct species comprising the following cytotoxic drug combination: A-Z which differ at least in mechanism of action and chemical structure such that one species could not be interchanged with another.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Note:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
2/7/06